VICH - GCP

99-045-1

Cy: Elsken

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Docket No. 99-045-1
Regulatory Analysis and Development
PPD, APHIS, Suite 3C03
4700 River Road
Riverdale, MD 20737-1238

re: Docket No. 99-045-1

Sir or Madam:

The following comments are submitted in response to the Notice published June 29, 1999 in the Federal Register. APHIS is proposing adoption of VICH "Guideline on Good Clinical Practices" (GCP) for veterinary biologic products. We believe that this guideline is appropriate for injectable biological products such as vaccines, toxins, etc., and see no problem with its adoption by APHIS.

IDEXX Laboratories, Inc., manufactures *in-vitro* diagnostics for detection of animal diseases. The GCP guideline specifically defines "Investigational Veterinary Product" (Sec. 1.15) as being "pharmaceutical," and having "active substances, " and being "administered or applied to an animal." As such, this guideline appears to be not applicable to *in-vitro* products. However, many *in-vitro* diagnostic products are considered as "analogous" to vaccines and other injectable products, and so are regulated as veterinary biologics under Title 9 of the Code of Federal Regulations. As such, we are concerned that *in-vitro* diagnostics would be covered by the GCP guideline, and that some inappropriate requirements might be imposed.

Many of the GCP requirements, especially as to organization of studies and integrity of data, are appropriate to any scientific enterprise, including investigations with *in-vitro* products. Some sections, however, relate to issues like care of treated animals or blinding of researches to study groups, and these should not be applied to research with *in-vitro* products. We request that when APHIS adopts this guideline, it should specifically exempt *in-vitro* products or make appropriate distinctions between injectable and *in-vitro* products. Doing this as part of adoption of the guideline will save considerable time in sorting out issues later when considering investigations for diagnostics.

Some of our specific concerns are in the following areas:

Adverse events are not easily defined for *in-vitro* diagnostics. Failure of a diagnostic to perform according to its claims would certainly be considered in determining whether to license a product, but should not be defined as an adverse event. Any definition of diagnostic adverse event relating to potential harm of subsequent medical decisions would be highly speculative.

We propose that the guideline exclude *in-vitro* diagnostics from any requirement that adverse events be monitored and reported.

Blinding / Masking are not really feasible relative to diagnostic methods. An investigator's staff could be blinded to the identity of the sample, but not to the method. Many diagnostics involve objective measurements (eg, optical density) so blinding should not be necessary in any case.

We propose that blinding or masking not be a requirement for diagnostic investigations. C4

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Informed Consent should not be required. For the most part, diagnostic investigations involve splits of samples taken for routine medical purposes; informed consent is usually not required for human studies in such cases. Even if samples are taken especially for a study, the sample acquisition procedure is usually routine. In either case, the animal is subject to insignificant or no additional risk.

We propose that *in-vitro* diagnostics should be exempted from this requirement, unless the animal is subject to some special treatment (beyond sample acquisition) as part of the study.

Care of Animals is not normally an issue with investigations of *in-vitro* products, so records showing appropriate care should not be required. Animals sampled may be sick or well, but they are not usually medicated, immunized, administered any special feeds or supplements, or subjected to any medical procedures as part of the diagnostic investigation. As stated above, the samples are usually splits from routine samples. A diagnostic study can be meaningful without animal care information because method-method comparisons and lot-lot reproducibility determinations are valid without information about the animal's condition.

As a practical matter, such records are not normally be available. Diagnostic specimens are most often provided by laboratories to which samples are sent by owners or veterinarians. Tracking animal care information for samples sent to labs would probably be impossible. Maintaining animals for the sake of the study would be prohibitively expensive and difficult.

We propose that for diagnostic investigations, there be no requirement to have, maintain, or provide records of care for the animals, except when the study calls for some special treatment of the animals.

Identity of the Sites can be provided under confidentiality to the regulatory authority, but should not be required in the protocol or the study report, which are likely to become public records. Many investigations are done at private companies who consider health status of their animals to be confidential business information. Often times, co-investigators are business competitors. As such, there is a real possibility that potential investigators would refuse to participate in a study if they perceive that comparative health information could be used to their detriment. With the consolidation of many animal production businesses, our ability to run studies could become seriously limited if producers will not take part in studies.

As such, we request that for diagnostic studies the protocol or study report should not required to identify the study sites.

Thank you for considering the above issues. Please feel free to contact us if you have any questions.

Sincerely,

Joseph W. O'Donnell
Senior Regulatory Affairs Specialist